EXAMINER'S AMENDMENT

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Mr. William H. Logsdon on 11/19/2010.

The instant claim 20 has been amended as follows:

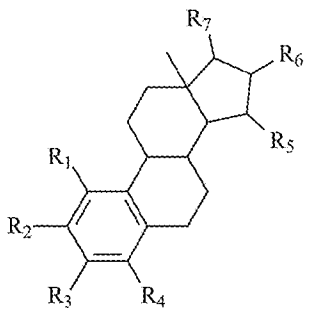
- at line 2, deletes the phrase "**at least**".

Reasons for Allowance

The following is an examiner's statement of reasons for allowance:

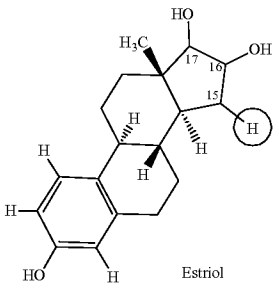
Claims 18-27 and 34-35 of the instant application are allowed.

Instant claims 18-27 and 34-35 are drawn to a method of treating or reducing the risk of developing an immune mediated disorder in a mammal selected from the group consisting of multiple sclerosis, rheumatic arthritis and osteoarthritis, wherein the method comprises administering a therapeutically effective amount of an estrogenic component as represented below (wherein the substituents R_5, R_6 and R_7 are hydroxyl groups):



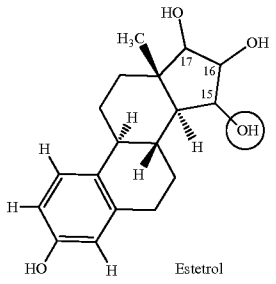
The instant invention has overcome the previous rejection under 35 U.S.C. § 112 first paragraph (Scope of Enablement) in that the instant claims have been amended to a method of treating or reducing the risk of developing an immune mediated disorder in a mammal selected from the group consisting of multiple sclerosis, rheumatic arthritis and osteoarthritis. Applicants provide data that utilized an experimental autoimmune encephalomyelitis (EAE) as an animal model for multiple sclerosis, in which the results showed that the administration of estetrol in an effective amount can alleviate symptoms in animals that are affected by encephalomyelitis (EAE) and prevent animals from developing a disease relapse with severe disease symptoms (see Specification: Examples 6-7). Applicants also utilized another animal model of autoimmune and chronic inflammatory disease for human arthritis diseases, such as rheumatoid arthritis, and the results showed that the administration of estetrol delay the onset of disease incidence as compared to the control group (see Specification: Examples 8-9).

In addition, the closest reference, namely Voskuhl, R. R. (see office action dated on 08/09/2007), recites a method of treating autoimmune related disease, more specifically Th-1 mediated autoimmune disease, such as multiple sclerosis or rheumatoid arthritis, by administering effective amount of steroid hormones to a mammal, wherein the steroid hormone is an estrogen or an estrogen receptor active agent, i.e. estriol (estra-1, 3,5(10)-triene-3, 16,17-triol or E3) represented by following structure:



Estriol

However, it is known that the additional hydroxy group present at the C-15 position of estetrol, as set forth below, greatly reduces its biological potency, possibly due to the altered polarity or molecular configuration of the compound and the increase in steric hindrance at the estrogenic receptor site (see Levine et al. Am. J. Obstet. Gynecol. 1984, March 15, page 738, left column and structures thereon). Therefore, the biological potency of the presently claimed estrogenic compounds, i.e. estetrol, for treating or reducing the risk of developing an immune mediated disorder would not have been obvious over the other naturally occurring estrogenic compounds based on its structural similarity with other known estrogens, i.e. estriol:



Estetrol .

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Contact Information

Any inquiry concerning this communication from the Examiner should direct to Helen Mei-Ping Chui whose telephone number is 571-272-9078. The examiner can normally be reached on Monday-Thursday (7:30 am – 5:00 pm). If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Johann Richter can be reached on 571-

272-0646. The fax phone number for the organization where the application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either PRIVATE PAIR or PUBLIC PAIR. Status information for unpublished applications is available through PRIVATE PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the PRIVATE PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/H. C./

Examiner, Art Unit 1616

/SREENI PADMANABHAN/

Supervisory Patent Examiner, Art Unit 1627